REMARKS / ARGUMENTS

In response to the office action of August 18, 2009, Applicant has amended the claims, which when considered with the following remarks and exhibits, is deemed to place the present application in condition for allowance. Favorable consideration of the presently amended claims is respectfully requested.

In the first instance, Applicant, through the undersigned, thanks Examiner Fubara, for the helpful comments made in a telephone interview held December 23, 2009. During the course of the interview, various amendments to the claims were proposed, among them, substituting "consisting of" for "comprising" in the preamble of claim 11 and/or deleting the phrase "and further optional pharmaceutically acceptable excipients". By this amendment, the preamble of claim 11 now recites "consisting" rather than comprising. Support for the amendments to claim 11 may be found throughout the specification, e.g., page 2, lines 9-27, and page 6, penultimate line to page 7, line 2.

In the office action of August 18, 2008, Claims 11, 12, and 14-20 have been rejected as allegedly unpatentable over Calne (US 5,212,155) and Posanski (GB 2 228 198 A) in view of Armistead et al. (U.S. 5,192,773) and Kao (US 5,262,423).

Calne has been cited for allegedly teaching a composition comprising rapamycin and pharmaceutically acceptable carriers including olive oil or alcohol or propylene glycol or surfactant such as cremophor for oral administration in the form of a tablet, caplet or capsule to inhibit transplant rejections. Calne is also relied upon for teaching that rapamycin can be used in combination with cyclosporin and one or more chemotherapeutic agents.

Posanski has been cited for allegedly teaching a pharmaceutical composition that contains cyclosporine, a carrier composition that contains oils, a tenside having a hydrophilic lipophilic balance (HLB) of at least 10, triglycerides, natural oils and glycerol monooleate. On page 4, item 11, of the office action, the Examiner has stated that "Posanski describes the carrier composition of claims 11, 14-17."

Applicant respectfully traverses the rejection for the following reasons. It is respectfully submitted that Posanski does not describe the carrier composition of claims 11 and 14-17. As

presently amended, feature (a) of claim 11 recites: "about 10-50% by weight, based on the carrier composition, of a sorbitan fatty acid ester co-surfactant which is substantially pure or which is in the form of a mixture of different sorbitan fatty acid esters, the co-surfactant having a hydrophilic-lipophilic balance of less than 10 (HLB value according to Griffin). Support for the amendment to feature (a) may be found throughout the specification, e.g., page 6, penultimate line, to page 7, line 2.

Posanski teaches at page 11, a pharmaceutical composition comprising:

a) a cyclosporin as active ingredient in a carrier medium comprising
b) a fatty acid triglyceride,
c) a glycerol fatty acid partial ester or propylene glycol (e.g., 1,2-propylene glycol) or sorbitol complete or partial ester, and
d) a tenside having a hydrophilic-lipophilic balance (HLB) or at least 10;

with the proviso as set forth therein.

Posanski never discusses feature c) apart from feature b); that is, fatty acid triglycerides and the sorbitol complete or partial ester are always discussed together. For example, the first full paragraph of Posanski on page 15 indicates that transesterification products are obtained by heating a vegetable oil, e.g., corn oil, with sorbitol at high temperature under an inert atmosphere with continuous agitation, to effect trans-esterification, e.g., sorbitolysis.

Posanski neither teaches nor suggests, a sorbitan fatty acid ester co-surfactant which is substantially pure or which is in the form of a mixture of different sorbitan fatty acid esters, the co-surfactant having a hydrophilic-lipophilic balance of less than 10 (HLB value according to Griffin). Rather, Posanski teaches a glycerol fatty acid partial ester or propylene glycol *or sorbitol complete or partial ester*. *See* page 11, item A of Posanski, reproduced above. The sorbitan fatty acid ester co-surfactant having an HLB of less than 10, recited in Applicant's claims 11 and 17 is distinct from the sorbitol complete or partial ester taught by Posanski. Applicant predicates this assertion on the following discussion.

In the first instance, an ester of a sorbitan is not the same as an ester of a sorbitol. See exhibit A, which provides a structural formula for sorbitol and Exhibit B which provides the structural formula for sorbitan. *See* also paragraphs [0002] and [0003] of US 2009/0012185

A1, provided herewith as Exhibit C, which indicates that sorbitan esters and sorbitol esters are different compounds.

Further, besides teaching a sorbitol complete or partial ester (and not a sorbitan ester presently recited in Applicant's claims), Posanski also teaches on page 15, third full paragraph, that when component (c), e.g., a sorbitol complete or partial ester, is obtained by trans-esterifcation of a vegetable oil with sorbital, it will also contain minor amounts of sorbitol as well as sorbitol mono-, di- and tetra-esters. *See also* page 16, second full paragraph of Posanski, which discloses sorbitol amounts of preferably less than 5% by weight, more preferably about 1 to 2% by weight; and the lower portion of page 17 of Posanski, which discloses that trans-esterification products of corn oil and sorbitol comprises free glycerol, free sorbitol, monoglycerides, diglycerides, triglycerides, as well as sorbitol mono-, di-, tri- and tetra-esters.

Nor does Calne teach or suggest a sorbitan fatty acid ester co-surfactant which is substantially pure or which is in the form of a mixture of different sorbitan fatty acid esters, the co-surfactant having a hydrophilic-lipophilic balance of less than 10 (HLB value according to Griffin) for use in a carrier composition.

Neither Armistead et al. nor Kao, teach or suggest a sorbitan fatty acid ester co-surfactant which is substantially pure or which is in the form of a mixture of different sorbitan fatty acid esters, the co-surfactant having a hydrophilic-lipophilic balance of less than 10 (HLB value according to Griffin) for use in a carrier composition. Thus, neither secondary reference can fill the gap of teaching/suggestion left by Calne and Posanski.

Summarizing, it is respectfully submitted that none of the cited references, taken separately, or in combination, teach or suggest a sorbitan fatty ester co-surfactant for use in a carrier composition. Nor is there any motivation provided by any of the references, taken separately or in combination, for preparing a carrier composition having such a co-surfactant.

In contrast, the present application clearly teaches on page 2, lines 9 through 27, that a sorbitan fatty acid ester co-surfactant having an HLB less than 10, is an essential element of the carrier composition. Examples of suitable sorbitan fatty acid esters for use in the present invention are set forth on page 7 of the present application where sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan tristearate, sorbitan monooleate,

sorbitan sesquioleate and sorbitan trioleate are listed. *See* **Table 16** of U.S. Pat. 6,923,988, provided as Exhibit A, in Applicant's amendment submitted August 7, 2008, which indicates that all of these sorbitan fatty ester surfactants have an HLB value of less than 10.

On page 5 of the office action, the Examiner has posited that Posanski teaches specific sorbitan, such as the palmitate, stearate, etc. on page 13, d2, and that therefore, it flows that the sorbitan of Posanski would have the number of saturated or unsaturated carboxylic atoms recited in claim 17. In response, Applicant respectfully submits that page 13, d2 of Posanski teaches use of a polyoxyethylene-sorbitan fatty acid ester, and not a sorbitan fatty acid ester as presently recited in the claims in this application. The sorbitan fatty acid ester co-surfactant having an HLB of less than 10, recited in the present claims, is distinct from the polyoxyethylene-sorbitan fatty acid esters listed on page 13, d2, of Posanski. As indicated therein, all of the polyoxyethylene-sorbitan fatty acid esters listed on page 13, d2, of Posanski are of the type known commercially as Tween® and such products have HLB values of greater than 10. Such polyoxyethylene fatty acid esters are disclosed on page 8 of the present application as component (c), as well as recited in the present claims as element (c) , i.e., a nonionic surfactant having an HLB value of more than 10.

As discussed above, none of the cited references taken separately or in combination, teach or suggest Applicant's essential claimed feature of a sorbitan fatty acid ester co-surfactant which is substantially pure or which is in the form of a mixture of different sorbitan fatty acid esters, the co-surfactant having a hydrophilic-lipophilic balance of less than 10 (HLB value according to Griffin) for use in a carrier composition. Such sorbitan fatty acid esters are commercially available under the registered trademarks Span®, Crill®, Dehymuls®, Fomodan® and Capmul®.

It remains well settled that obviousness requires at least a suggestion of all of the features in a claim. When determining whether a claim is obvious, an examiner must make "a searching comparison of the claimed invention – *including all its limitations* – with the teaching of the prior art." *In re Ochiai*, 71 F.3d 1565, 1572, 37 USPQ2d 1127,1132 (Fed. Cir. 1995) (emphasis added). Thus, "obviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (*citing In re Royka*, 490 F.2d 981, 985, 180 USPQ 580 (CCPA 1974)). Moreover, as the Supreme Court recently stated, "*there must be some articulated reasoning* with some rational underpinning to support

the legal conclusion of obviousness." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting In re Kahn, 441 F.3d 977, 988 (Fed. Cir. 2006) (emphasis added)).

Applicant respectfully submits that since the combination of cited prior art references does not suggest all the features of Applicant's independent claims (as fully discussed above in relation to the sorbitan fatty acid ester co-surfactant), the subject matter of claims 11, 12 and 14-40 is not obvious. Accordingly, the rejection of claims 11, 12 and 14-40 under 35 U.S.C. §103(a) should be withdrawn.

Claims 11, 12 and 14-20 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over Claims 11-19 of copending Application No. 10/961,785 in view of Armistead et al. (US Pat. 5,192,773) and Kao (US Pat. 5,262,423) and further in view of Posanski (GB 2 228 198 A).

Claims 11, 12 and 14-20 have also been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over Claims 11-22 of copending Application No. 10/623,887.

In response to the double patenting rejection, a terminal disclaimer will be submitted forthwith, disclaiming that portion of the term of any patent issuing from the present application that would extend past the term of the first to expire of any patent issuing from U.S. application No. 10/961,785 and Application No. 10/623,887. Upon the Examiner's receipt of the terminal disclaimer, withdrawal of the double patenting rejection is respectfully requested.

In view of the foregoing remarks, exhibits and amendments, and upon receipt of the terminal disclaimer, it is respectfully submitted that the pending claims are in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

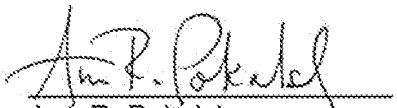

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EXHIBIT A

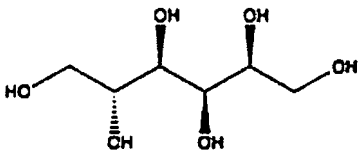
Sorbitol

From Wikipedia, the free encyclopedia

Sorbitol, also known as **glucitol**, is a sugar alcohol that the human body metabolises slowly. It is obtained by reduction of glucose changing the aldehyde group to an additional hydroxyl group.

Contents

- 1 Uses
  - 1.1 Sweetener
  - 1.2 Laxative
  - 1.3 Medical applications
  - 1.4 Health care, food, and cosmetic uses
- 2 Medical importance
- 3 Adverse medical effects
- 4 Overdose effects
- 5 Compendial status
  - 5.1 Other uses
- 6 See also
- 7 External links
- 8 Notes and references

Sorbitol	
	
IUPAC name	(2S,3R,4R,5R)-Hexane-1,2,3,4,5,6-hexol
Other names	D-glucitol D-Sorbitol
Identifiers	
CAS number	50-70-4 ✓
PubChem	82170
MeSH	Sorbitol
SMILES	O[C@H]([C@H](O)CO)[C@H](O)[C@@H](O)CO
Properties	
Molecular formula	$C_6H_{14}O_6$
Molar mass	182.17 g mol^{-1}
Density	1.489 g/cm^3
Melting point	95 °C
Boiling point	296 °C
✓ (what is this?) (verify) Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)	
Infobox references	

Uses

Sweetener

Sorbitol is a sugar substitute. It may be listed under the inactive ingredients listed for some foods and products. Sorbitol is referred to as a nutritive sweetener because it provides dietary energy: 2.6 kilocalories (11 kilojoules) per gram versus the average 4 kilocalories (17 kilojoules) for carbohydrates. It often is used in diet foods (including diet drinks and ice cream), mints, cough syrups, and sugar-free chewing gum.

It also occurs naturally in many stone fruits and berries from trees of the genus *Sorbus*.[1]

Laxative

Sorbitol can be used as a non-stimulant laxative via an oral suspension or enema. It works by drawing water into the large intestine, thereby stimulating bowel movements.[2] Sorbitol has been determined safe for use by the elderly, although it is not recommended without consultation with a clinician.[3]

EXHIBIT B

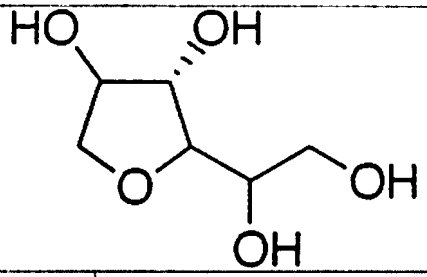
Sorbitan

From Wikipedia, the free encyclopedia

Sorbitan is a mixture of chemical compounds derived from the dehydration of sorbitol. The mixture can vary, but usually consists of 1,4-anhydrosorbitol, 1,5-anhydrosorbitol and 1,4,3,6-dianhydrosorbitol.[1] Sorbitan is primarily used in the production of surfactants such as polysorbates.

Sorbitan esters (also known as Spans) are lipophilic non ionic surfactants that are used as emulsifying agents in the preparation of emulsions, creams, and ointments for pharmaceutical and cosmetic use. When used alone they produce stable water-in-oil emulsions but they are frequently used with a polysorbate (also known as Tweens) in varying proportions to produce water-in-oil or oil-in-water emulsions or creams with a variety of different textures and consistencies. Sorbitan esters are also used as emulsifiers and stabilisers in food. [2]

Sorbitan



IUPAC name	(3*S*)-2-(1,2-Dihydroxyethyl) tetrahydrofuran-3,4-diol
Identifiers	
CAS number	12441-09-7
PubChem	103023
SMILES	C1C([C@@H](C(O1)C(CO)O)O)O
Properties	
Molecular formula	$C_6H_{12}O_5$
Molar mass	164.16 g/mol
Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)	
Infobox references	

References

1. ^ *Merck Index*, 12th Edition, **8872.**
2. ^ Martindale: The Complete Drug Reference © 2005 The Pharmaceutical Press.

EXHIBIT C

SURFACTANT COMPOSITION

FIELD OF INVENTION

[0001] The present invention relates to a surfactant composition comprising a sorbitan ester and a sorbitol ester, to an emulsion formed using the surfactant composition, and in particular to a personal care or cosmetic product formed from the emulsion.

BACKGROUND

[0002] Sorbitan esters have been used for many years as surface active agents, having emulsifying, dispersing, wetting and/or solubilising properties in a wide range of applications such as personal care, cleaning, general industrial, food, and many others. In particular, sorbitan esters have been used as emulsifiers in personal care applications, for example skin care, sunscreens, toiletries, decorative cosmetics, perfumes and fragrances.

[0003] Commercial production of sorbitan esters normally involves the reaction of sorbitol with fatty acids or derivatives thereof, and results in a complex mixture of products including sorbitol mono-, di-, tri-, and higher esters, sorbitan mono-, di-, and higher-esters, isosorbide mono-, and di-esters, and non-esterified sorbitol, sorbitan and isosorbide. The concentrations of the aforementioned individual components can vary, but sorbitan esters are the main components. There can be significant amounts of isosorbide esters present, but sorbitol esters are normally present at very low concentrations. The number of carbon atoms present in the hydrophobe of the sorbitol/sorbitan/isosorbide esters is dependant upon the particular fatty acid(s) employed in the reaction, and the average number thereof will be substantially the same for all of the components.

[0004] Current commercially available sorbitan esters are effective emulsifiers in many applications, but there is still a requirement to improve the properties thereof, particularly in personal care applications, such as flexibility of use, improved water resistance, smooth and light skin feel, and spreading properties. Often an additional co-emulsifier is required to be used with sorbitan esters, and there would be significant advantages if a sorbitol based self-emulsifying system could be developed, i.e. without the need for a co-emulsifier, particularly one capable of forming liquid crystals in water, and especially in oil in water emulsions.

SUMMARY OF THE INVENTION

[0005] We have now surprisingly discovered a surfactant composition which overcomes or significantly reduces at least one of the aforementioned problems.

[0006] Accordingly, the present invention provides a surfactant composition comprising at least one sorbitan ester and at least one sorbitol ester wherein the mean number of carbon atoms of the hydrophobe of the sorbitan ester is greater than that of the sorbitol ester.

[0007] The invention also provides a method of forming a surfactant composition which comprises mixing together a sorbitan ester component and a sorbitol ester component wherein the mean number of carbon atoms of the hydrophobe of the sorbitan ester is greater than that of the sorbitol ester.

[0008] The invention further provides an emulsion comprising a surfactant composition capable of forming liquid crystals in water which comprises at least one sorbitan ester and at least one sorbitol ester wherein the mean number of carbon atoms of the hydrophobe of the sorbitan ester is greater than that of the sorbitol ester.

[0009] The invention further provides a personal care or cosmetic product comprising a surfactant composition comprising at least one sorbitan ester and at least one sorbitol ester wherein the mean number of carbon atoms of the hydrophobe of the sorbitan ester is greater than that of the sorbitol ester.

[0010] The invention still further provides the use of a surfactant composition comprising at least one sorbitan ester and at least one sorbitol ester wherein the mean number of carbon atoms of the hydrophobe of the sorbitan ester is greater than that of the sorbitol ester, to stabilise an emulsion.

[0011] The invention yet further provides the use of a surfactant composition comprising at least 3% by weight of at least one sorbitol ester, to form liquid crystals in the water phase of an oil in water emulsion, to stabilise the emulsion.

[0012] The sorbitan and/or sorbitol esters used in the present invention are normally made by reacting sorbitol with fatty acids or derivatives thereof, e.g. fatty acid methyl, ethyl and/or isopropyl esters, or fatty acid triglycerides. Preferred fatty acids comprise in the range from 8 to 24, more preferably 10 to 22, particularly 12 to 20, and especially 12 to 18 carbon atoms. Linear fatty acids are preferred. Suitable fatty acids include capric, lauric, myristic, palmitic, stearic, and/or behenic acid.

[0013] In a preferred embodiment greater than 80%, more preferably greater than 85%, particularly greater than 90%, and especially greater than 95% by weight of saturated fatty acids are employed. The concentration of unsaturated fatty acids used is preferably less than 20%, more preferably less 15%, particularly less than 10%, and especially less than 5% by weight. Oleic acid is a particularly suitable unsaturated fatty acid.

[0014] The mean number of carbon atoms (on a molar basis) present in the hydrophobe (derived from the fatty acid or derivative thereof) of the sorbitan esters is suitably at least 1, preferably at least 2, more preferably in the range from 3 to 7, particularly 4 to 6, and especially 4.5 to 5 greater than the mean number of carbon atoms present in the hydrophobe of the sorbitol esters. The mean number of carbon atoms of the sorbitan ester hydrophobe is suitably in the range from 12 to 24, preferably 14 to 20, more preferably 15 to 19, particularly 16 to 18, and especially 16.5 to 17.5. The mean number of carbon atoms of the sorbitol ester hydrophobe is suitably in the range from 8 to 20, preferably 10 to 16, more preferably 11 to 14, particularly 11.5 to 13, and especially 12 to 12.5.

[0015] The ratio of sorbitan esters to sorbitol esters present in a composition according to the present invention is suitably in the range from 1 to 50:1, preferably 2 to 30:1, more preferably 4 to 20:1, particularly 7 to 13:1, and especially 9 to 11:1 by weight.

[0016] The concentration of sorbitan esters is suitably in the range from 25 to 95%, preferably 45 to 90%, more preferably 60 to 85%, particularly 65 to 80%, and especially 69 to 73% by weight of the total composition. The concentration of sorbitol esters is suitably in the range from 1 to 25%, preferably 3 to 15%, more preferably 5 to 12%, particularly 7 to 9%, and especially 7.5 to 8.5% by weight of the total composition. The concentration of isosorbide esters is suitably in the range from 3 to 35%, preferably 7 to 25%, more preferably 10 to 20%, particularly 14 to 18%, and especially 15 to 17% by weight of the total composition.

[0017] Suitable sorbitan esters include sorbitan cocoate, sorbitan caprate, sorbitan laurate, sorbitan myristate, sorbitan